HFI-35

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DEPARTMENT OF HEALTH & HUMAN SERVICES
New York District

Food & Drug Administration
850 Third Avenue
Brooklyn, NY 11232

WARNING LETTER

January 7, 1999

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

REF: NYK-1999-20

Dr. Joseph J. Fink
President
Plastodent, Inc.
2881 Middletown Road
Bronx, New York 10461

Dear Dr. Fink:

During an inspection of your drug manufacturing facility on November 17, 19, 20 & 30 and December 7 & 14, 1998, our investigator documented deviations from Current Good Manufacturing Practice (CGMP) for Finished Pharmaceuticals Regulations [Title 21, Code of Federal Regulations, Parts 210 and 211] concerning the manufacture of your drug products Sodium Fluoride Oral Solution, Benzocaine Gel and Tolnaftate Antifungal Powder for Athlete's Foot. These deviations cause these drug products to be adulterated within the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). The deviations include, but are not limited to, the following:

(1) Failure to test an adequate number of batches of each drug product to determine an appropriate expiration date in accordance with 21 CFR 211.166 (b). For example, review of stability data for your prescription drug, Sodium Fluoride Oral Solution, U.S.P., 30 ml. revealed only two lots of this product had been tested for stability. One lot was tested after three years at room temperature, and the second lot had only been tested after one year at room temperature and 3 months at accelerated temperatures.

In addition, stability test records for Sodium Fluoride Oral Solution and Benzocaine Gel 20% Topical Anesthetic revealed test intervals were not scheduled. Intervals were irregular at 3 months

accelerated, 1 year at room temperature and then 3 years at room temperature with no testing in between these intervals.

(2) Failure to establish an adequate written testing stability program designed to assess the stability characteristics of drug products in accordance with 21 CFR 211.166 (a) in that your program has the following deficiencies:

A. Sample size is not addressed.

B. Test intervals are indicated as ranges of time depending on the length of the stability requirements. There are no specific instructions regarding test schedules for each drug.

C. Your procedures indicate storage is to be at controlled room temperature and humidity, but there are no procedures for the control of temperature or humidity nor any equipment for this purpose.

(3) Failure to have equipment for adequate control of temperature as required by 21 CFR 211.46 (b) in that:

A. There is no thermometer or temperature recording instrument in the area of finished product storage to assure that product is stored within labeled temperatures to assure that the identity, strength, quality and purity of these drug products are not affected.

B. There are no thermometers, thermostats, etc. to monitor or control proper temperature for stability samples as was observed for samples of Sodium Fluoride Oral Solution and Topical Anesthetic.

(4) Failure to conduct operations within specifically defined areas of adequate size. Your facility does not have separate or defined areas or control systems for firm operations as are necessary to prevent contamination or mixups during all points of operation as required by 21 CFR 211.42 (c). For example:

During the course of the inspection, the investigator observed packaging of Antifungal Powder for Athlete's Foot from open drums of bulk raw material powder. These open drums were within one foot of open drums of the raw materials [redacted] Isopropyl Myristate and [redacted] Poly Oxyethylene Polyol Fatty Acid Ester. During the course of this packaging operation, excessive dusting of the material being packaged was observed in the area. It was also noted that the finished product, Antifungal Powder for Athlete's Foot and raw materials [redacted] Isopropyl Myristate and [redacted] Poly Oxyethylene Polyol Fatty Acid Ester were stored in the same area and bore printed container labels obscured with a layer of thick product dust.

(5) Failure to maintain your facility in a clean and sanitary condition free of infestation by rodent or other vermin as required by 21 CFR 211.56 (a), in that a live mouse was observed moving across the first floor from one of the packaging rooms to another manufacturing/ production area.

(6) Your firm currently uses the unacceptable procedure of human mouth suctioning to siphon raw materials from bulk containers into the [redacted] manufacturing filling machine to manufacture Tolnaftate Topical Solution. There are no written procedures designed to assure that components are handled in a manner to prevent contamination as required by 21 CFR 211.80 (b).

(7) Failure to maintain complete records of the periodic calibration of laboratory instruments in accordance with 21 CFR 211.194 in that there are no calibration records for the [redacted] small [redacted] balance beam scales, the [redacted] balance scales or the analytical scale.

(8) Failure to maintain records of equipment maintenance as required by 21 CFR 211.67 (c) in that there were no maintenance records for your firm's [redacted] blenders, [redacted] ball mixers, [redacted] drum heaters, [redacted] paste tube mixing machines and [redacted] large paste tube filling machines.

(9) Failure to store labels and other labeling materials for each different drug product, strength, dosage form or quantity of contents separately with suitable identification and with limited access to authorized personnel in accordance with 21 CFR 211.122 (d). For example, the cabinet utilized for the storage of labels is not organized in a manner that would prevent label mix-up. Labels for several drug products were observed to be stored in a disorganized manner, unstacked, unidentified, unbounded, etc. These labels included labels for Sodium Fluoride Oral Solution USP 30 ml. and Topical Anesthetic 20% Benzocaine Gel.

(10) Failure to assure that personnel engaged in the manufacture, processing, packing or holding of drug products wear clean clothing appropriate for the duties they perform in accordance with 21 CFR 211.28 (a). Protective apparel, such as head, face, hand, and arm coverings are required to be worn as necessary to protect drug products from contamination. During the inspection, several employees working in the manufacturing and packaging areas wore no protective gowns, head or hand coverings.

(11) Failure to include a statement of theoretical weight or measure at appropriate phases of processing in master production records as required by 21 CFR 211.186 (b) (7) as observed in master records for Sodium Fluoride Oral Solution USP 30 ml, Topical Benzocaine Anesthetic Gel 20% and Tolnaftate Powder USP 1%.

(12) Failure to include sampling, testing procedures and specifications regarding in process testing in the master records for Sodium Fluoride Oral Solution, Benzocaine Gel and Tolnaftate Powder as required by 21 CFR 211.186 (b).

(13) Failure to establish written procedures designed to set forth the responsibilities and procedures applicable to the quality control unit in accordance with 21 CFR 211.22 (d).

(14) Failure to establish written procedures for the annual review of quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures in accordance with 21 CFR 211.180 (e). Written procedures must be established and followed for such evaluations and shall include provisions for the review of a representative number of batches, and the review of complaints, recalls, returned or salvaged drug products and any investigations.

(15) Failure to establish written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures as required by 21 CFR 211.80 (a). For example:

A. Your written procedures fail to address the specific manner in which samples are to be collected, as well as the quantity.

B. Your procedures direct that at least one identity test be conducted, but the test is not described or referenced.

C. Your procedures indicate that containers and closures shall be visually identified rather than processed in the same manner as raw materials, i.e. sampled, examined to meet specifications and released.

D. Your procedures describe a coded tag to be used to identify materials quarantined, approved or rejected, but the procedure fails to identify the codes for each of these designations.

(16) Failure to establish adequate written procedures describing the handling of all written and oral complaints regarding drug products in accordance with 21 CFR 211.198. For example, your written procedures lack specific directives and consist only of a form with no provision for recording the name of the complainant or any reply.

(17) Failure to establish adequate written procedures for the cleaning and maintenance of equipment used in the manufacture, processing, packing or holding of a drug product as required by 21 CFR 211.67 (b) in that your procedures fail to indicate an amount of IPA cleaning solution and water to be used for cleaning. The procedures lack specific directives as to how the cleaning is to be performed.

(18) Failure to establish written procedures describing a system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary in accordance with 21 CFR 211.150 (b).

(19) Failure to maintain written procedures for the use of suitable rodenticides, insecticides, fungicides, fumigating agents and cleaning and sanitizing agents in accordance with 21 CFR 211.

56 (c). Such procedures are designed to prevent the contamination of equipment, components, drug product containers, closures, packaging, labeling materials or drug products.

Neither the above identification of CGMP violations nor the inspectional observations (Form FDA 483) (copy enclosed) presented to you at the conclusion of the inspection is intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence with each requirement of the Act and its implementing regulations. Federal agencies are advised of the issuance of all warning letters about drug products so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or injunction.

You should notify this office in writing, within 15 working days of receipt of this letter, of (1) each step that has been or will be taken to completely correct the current violations and to prevent the recurrence of similar violations; (2) the time within which the corrections will be completed; (3) any reason why the corrective action has not been completed within the response time; and (4) any documentation necessary to show the corrections have been achieved.

Your reply should be sent to the attention of Lillian C. Aveta, Compliance Officer, Food and Drug Administration, 850 Third Avenue, Brooklyn NY 11232, Tel. (718) 340-7000, ext. 5142.

Sincerely,

Brenda J. Holman
District Director

Attachment: Form FDA 483 dated 11/17, 19, 20 & 30/98 & 12/7 & 14/98